Claims

1. A method of regulating cytotrophoblast differentiation and migration characterized by regulating the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF-β by administration of any of IGF-II, IGF-II analogues, or antibodies specific against latent TGF-β to thereby promote the interaction between IGF-II and CIM6P.

2. A method of promoting the implantation of an embryo in the uterine decidual endometrium, characterized by regulating the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF-β by administration of any of IGF-II, IGF-II analogues, or antibodies specific against latent TGF-β to thereby promote the interaction between IGF-II and CIM6P.

3. A method according to claim 2, characterized in that IGF-II, IGF-II analogues, or antibodies specific against latent TGF-β that promote the interaction between IGF-II and CIM6P are administered to an embryo produced by in vitro fertilization.

4. A method according to claim 2, characterized in that IGF-II, IGF-II analogues, or antibodies specific against latent TGF-β that promote the interaction between IGF-II and CIM6P is administered to a pregnant female subject in need thereof.

5. A method according to claim 2, characterized in that IGF-II, IGF-II analogues, or antibodies specific against latent TGF-β that promote the interaction between IGF-II and CIM6P is administered to a pregnant female subject in the first half of pregnancy.

6. A method according to claim 2 characterized in that IGF-II, IGF-II analogues, or antibodies specific against latent TGF-β that promote the interaction between IGF-II and CIM6P are administered whilst maintaining the embryo in a relatively hypoxic environment.

7. A method according to claim 1 or claim 2, characterized in that the embryo is a mammalian embryo selected from human, horse, cow, pig, goat or sheep.

8. A method of preventing the implantation of an embryo in the uterine decidual endometrium, characterized by regulating the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF-β by administration of latent TGF-β or analogues or antibodies specific against IGF-II that inhibit the interaction between IGF-II and CIM6P.

9. A method of regulating differentiation and migration of embryonic stem cells or adult stem cells characterized by regulating the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF-β by administration of any of IGF-II, IGF-II analogues, or antibodies specific against latent TGF-β that promote the interaction between IGF-II and CIM6P.

10. A method of promoting terminal differentiation of embryonic stem cells or adult stem cells characterized by regulating the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF-β and exposing said cells to reduced levels of IGF-II, such that the stem cell CIM6P receptors are able to bind latent TGF-β and thereby promote the activation of TGF-β.

11. A method of promoting stem cell division and stem cell migration characterized by regulating the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF-β and exposing said cells to increased levels of IGF-II, such that the stem cell CIM6P receptors are unable to bind latent TGF-β and thereby inhibiting the activation of TGF-β.

12. A method of diagnosing a predisposition of cytotrophoblast cells or stem cells to differentiate and migrate, characterized by determining in the mother, father or embryo the presence of a polymorphic form of a gene wherein the level of expression of the gene serves to regulate the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF-β and, such that the CIM6P receptors have altered ability to bind latent TGF-β and thereby altered ability to activate TGF-β.

13. A method according to claim 12, characterized in that the gene is selected from an insulin-like growth factor II gene, a urokinase plasminogen activator gene, a urokinase plasminogen activator receptor gene, a CIM6P (type-2 IGF) receptor gene, a TGFβ gene, a plasminogen gene or any polymorphic forms thereof.

14. A method of diagnosing a predisposition of cytotrophoblast cells to differentiate and migrate, characterized by determining in the mother, father or embryo the sequence of nucleotides in the DNA near the insulin-like growth factor II gene known as the insulin (*INS*) variable number of tandem repeats (VNTR), to thereby determine the capacity of the cytotrophoblast cells to synthesize IGF-II and thus the capacity of the cytotrophoblast to migrate into the uterine decidua and the capacity of the placenta to transport substrates to the embryo.

15. A method of determining the ability of cytotrophoblast cells to differentiate and migrate, characterized by measurement of the amount of messenger RNA transcribed from the insulin-like growth factor II gene in embryos.

16. A method of determining the ability of cytotrophoblast cells to differentiate and migrate characterized by measurement of the amount of insulin-like growth factor II protein secreted by mammalian embryos.

17. A method of determining the ability of cytotrophoblast cells to differentiate and migrate characterized by measurement of the amount of insulin-like growth factor II protein circulating in maternal and paternal blood.